PART I.
ORGANOMETALLIC COMPOUNDS DERIVED FROM 3,3′-DIBROMOBIPHENYL

PART II.
THE SYNTHESIS OF 3-METHOXYHOMOPHTHALIC ACID

BY

CLIFFORD DANIEL MARSHALL

B.S., Southern Methodist University, 1942

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
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PART I.

ORGANOMETALLIC COMPOUNDS DERIVED FROM 3,3′-DIBROMOBIPHENYL

Introduction

In connection with work in this laboratory on another problem several unsuccessful attempts to prepare organometallic derivatives from 3,3′-dibromobiphenyl were made. The dibromobiphenyl employed in those experiments had been made from *o*-nitrobromobenzene by reduction to the hydrazo compound, rearrangement to the benzidine, and deamination. Although the dibromobiphenyl so prepared had the melting point previously reported for a sample of the 3,3′-isomer made by the Ullmann reaction, the intermediate hydrazo compound and benzidine had properties different from those previously ascribed to these substances. Accordingly, the structure of the supposed 3,3′-dibromobipehnyl cannot be regarded as established. Since there is no reason to believe that pure 3,3′-dibromobiphenyl cannot be converted to organometallic derivatives, the present study was directed toward a reëxamination of the structure of the compound and its behavior toward metals and organometallic reagents.

Discussion Of Results

3,3′-Dibromobenzidine prepared by the direct bromination of N,N′-diacetylbenzidine (1) was found to be indistinguishable from the product that is formed from *o*-nitrobromobenzene by reduction to the hydrazo compound and rearrangement to the benzidine (2). In a Sandmeyer reaction with cuprous bromide the tetrazonium salt from the dibromobenzidine (prepared from *o*-nitrobromobenzene) gave a product possessing the same melting point as the 3,4,3′,4′-tetrabromobiphenyl obtained by van Roosmalen (3) from a dibromobenzidine prepared by the direct bromination method.

Preliminary experiments on the formation of the Grignard reagent of 3,3′-dibromobiphenyl revealed that under normal conditions for Grignard preparations no reaction took place. Thus, the addition of a crystal of iodine, or of a trace of a low molecular weight alkyl bromide did not serve to initiate the reaction, and neither was the use of an activated magnesium nor of Gilman's activated copper-magnesium alloy to any avail. However, when preformed ethylmagnesium bromide was employed the difunctional Grignard reagent was formed as shown by its conversion upon carbonation to the known 3,3′-biphenyldicarboxylic acid (4). When the Grignard preparation was carried out with only one equivalent of magnesium, both the mono- and difunctional organometallic compounds were formed as shown by the conversion to the mono- and dibasic acids.

3,3′-Dibromobiphenyl could not be induced to react with metallic lithium; however, it did react with *n*-butyllithium to produce the difunctional organometallic compound, the presence of which was demonstrated by carbonation.

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PART II.

THE SYNTHESIS OF 3-METHOXYHOMOPHTHALIC ACID

Introduction

Recent studies of yohimbine and of certain of the curare

alkaloids indicate that these substances contain the ring system of 1,2-(2,3-naphtho)-β-carboline. It is to be expected that compounds having this nucleus might be synthesized from tryptamine and derivatives of homophthalic acid. 3-Methoxyhomophthalic acid is of particular interest in this connection because it should lead to compounds having the carboxyl and methoxyl groups in the same positions as the functional groups occupy in yohimbine. The purpose of the present work was to develop a synthetic route to 3-methoxy-homophthalic acid that would provide the compound in a reasonably good yield.

Discussion Of Results

3-Methoxyhomophthalic acid has been synthesized from 3-methoxyhydrocinnamic acid by the series of reactions discussed below. 3-Methoxyhydrocinnamic acid was brominated in either glacial acetic acid or chloroform to 6-bromo-3-methoxyhydrocinnamic acid, whose structure was proved. 4,6-Dibromo-3-methoxyhydrocinnamic acid was formed as a by-product.

6-Bromo-3-methoxyhydrocinnamyl chloride was cyclized to 4-bromo-7-methoxy-1-hydrindone by aluminum chloride in the following solvents: benzene, nitrobenzene, *sym.*-tetrachloroethane, and a mixture of the last two named solvents. The best yield of the hydrindone was realized when the solvent mixture was employed; when carbon disulfide was the solvent, 4-bromo-7-hydroxy-1-hydrindone was the product formed. The methoxyhydrindone and a dimeric compound were produced when polyphosphoric acid was the cyclizing agent. Liquid hydrogen fluoride failed to effect cyclization in good yield, and stannic chloride failed to yield any of the hydrindone.

Ethyl acetate-methanol was found to be the best solvent for the formation of 4-bromo-7-methoxy-2-isonitroso-1-hydrindone by the action of methyl nitrite on the 1-hydrindone.

The Beckmann rearrangement of the 2-isonitroso compound by means of thionyl chloride, thionyl chloride in chloroform,

or phosphorous pentachloride in ether gave a product which could be hydrolyzed to 6-bromo-3-methoxyhomophthalic acid.

In one experiment employing thionyl chloride in chloroform 6-bromo-2-carboxy-3-methoxyphenylacetonitrile was isolated, and in another, 5-bromo-1-chloro-3-hydroxy-8-methoxyisoquinoline.

3-Methoxyhomophthalic acid was obtained from 6-bromo-3-methoxyhomophthalic acid by refluxing an alkaline solution of the latter compound with Raney nickel catalyst.

A series of projected reactions which involve the use of 3-methoxyhomophthalic acid as a point of departure has been discussed.

VITA

The author was born on May 27, 1921, in Dallas, Texas, where he attended the public schools, being graduated from Forest Avenue High School in June, 1938. In September of that same year he entered Southern Methodist University, from which institution he was granted the Bachelor of Science Degree in 1942. After having worked for one year as a Junior Chemist with the Tennessee Valley Authority at Muscle Shoals, Alabama, he spent three years in the Naval Reserve of the United States. In September, 1946, he entered the Graduate College of the University of Illinois, where he was part time teaching assistant from 1947 to 1948 and a University Fellow for the academic year 1948-1949.

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